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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/976,935

Applicant(s)

STAUNTON, DONALD E.

Examiner

John S. Brusca

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) 6,8,9,18,19,22-25,30-32,36-47 and 49 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7,10-17,20,21,26-29,33-35 and 48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 3-5, 7, 12-17, 20, 21, 26-29, 33-35, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 35 and 48 are drawn to a method of contacting FtsZ protein with an effector that interacts with an allosteric regulatory site of the protein and modulates binding of the protein with a binding partner. In some embodiments the effector of the FtsZ protein is a small molecule, a diaryl compound, a diarylamide, or a diarylsulfide compound. In one embodiment the binding partner is GTP.

The specification describes in Table 1 on pages 30-66 96 classes of proteins with alpha beta structures. The specification describes 17 working examples of methods of modulating binding of first molecules as claimed:

- 1) CD11B in example 3, pages 87-89 and example 16, pages 127-128
- 2 and 3) C2 and factor B in example 4, pages 89-96
- 4-11) seven integrins in example 9, pages 107-111 (see Table 5, page 111)
- 12-13) two integrins in example 11, pages 114-116

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14) alpha 1 integrin in example 12, pages 116-122

15) Rac 1 in example 17, pages 128-131

16) HPPK in example 19, pages 133-141.

17) ENR in example 21, pages 143-145

The description of methods using 17 proteins in the specification does not include a description of a method of modulation of binding of FtsZ protein. The specification shows in example 20 on pages 142-143 a prophetic example of a FtsZ binding assay, and describes FtsZ on page 19, and further lists FtsZ in table 3 on page 84 as having sufficient similarity to allosteric proteins to classify FtsZ protein as an allosteric protein. However the specification does not describe effectors of any type of FtsZ. The specification does not describe a method utilizing FtsZ that comprises effectors, or the structural limitations of an FtsZ effector such as small molecule, diaryl compounds, and diarylamide or diarylsulfide structures.

Claims 3-5, 7, 12-17, 20, 21, 26-29, 33-35, and 48 are drawn to methods of using allosteric effector molecules that are diarylamide compounds. Amides are compounds with an acyl group linked to an NH₂ group. The specification does not show a structure or describe a working example of a diarylamide effector that regulates binding as part of the claimed method.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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4. Claims 1, 2, 4, 5, 7, 10, 11, 13-17, 20, 21, and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamilton et al. in light of Lee et al.

The claims are drawn to a method of using an effector that modulates the binding of a protein that comprises an alpha/beta domain and an allosteric regulatory site to a binding partner. In some embodiments the effector is a small molecule, or is a diaryl compound. In some embodiments the protein comprises a Rossmann fold structure in a 321456, 231456, or a 32145 orientation. In some embodiments the effector decreases binding between the protein and the binding partner.

Hamilton et al. shows in the abstract and throughout compounds that inhibit binding of the integrin Mac-1 to neutrophils. On page 1652 Hamilton et al. shows that the binding is contributed by Mac-1 in two assays. Platelet activating factor (PAF) activated neutrophils were blocked from binding serum coated plastic wells by anti-Mac-1 antibodies, and tumor necrosis factor (TNF) activated neutrophils were blocked from binding serum coated plastic wells by anti CD11b antibodies (Mac-1 comprises CD11b and CD18). Hamilton et al. assayed a number of small molecules for effect on binding of PAF and TNF treated neutrophils in tables 1-4. Compounds 4-9 in table 1, 10-22 in table 2, and compounds 23, 24, and 26 in table 3 are diaryl small molecules that inhibit binding of TNF activated neutrophils. Compounds 11, 17, 19, 22, NPC 15669, and NPC 17923 in Table 4 are diaryl small molecules that inhibit binding of PAF activated neutrophils.

Lee et al. shows in the abstract and throughout the structure of two conformations of the integrin Mac-1 I domain. Lee et al. shows on page 1334 that Mac-1 comprises a Rossmann fold

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and an I domain. Figure 4 shows that the I domain comprises alpha helical and beta sheet regions.

Regarding the allosteric regulatory site, the specification defines allosteric proteins as proteins with a high level of similarity to proteins that are known allosteric proteins in Example 1, pages 81-83. On table 3, page 84, the specification identifies Mac-1 as an allosteric protein. The claimed method limitations that are not explicitly described Hamilton et al. are inherent properties of Mac-1 as discussed above. The MPEP states in 2112.01:

V. ONCE A REFERENCE TEACHING PRODUCT APPEARING TO BE
SUBSTANTIALLY IDENTICAL IS MADE THE BASIS OF A REJECTION,
AND THE EXAMINER PRESENTS EVIDENCE OR REASONING
TENDING TO SHOW INHERENCY, THE BURDEN SHIFTS TO THE
APPLICANT TO SHOW AN UNOBVIOUS DIFFERENCE

“[T]he PTO can require an applicant to prove that the prior art products do not
necessarily or inherently possess the characteristics of his [or her] claimed product.

Whether the rejection is based on inherency’ under 35 U.S.C. 102, on prima facie
obviousness’ under 35 U.S.C. 103, jointly or alternatively, the burden of proof is the
same...[footnote omitted].” The burden of proof is similar to that required with respect to
product-by-process claims. In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596
(CCPA 1980) (quoting In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34

(CCPA 1977)).

Response to Arguments

5. Applicant's arguments filed 21 August 2006 have been fully considered but they are not persuasive.

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The applicants state that the Rossmann fold of FtsZ is described in the specification because a publication by Nogales et al. is mentioned on pages 19 and 142, This portion of the specification does not describe a FtsZ protein with a Rossmann fold because although the specification does mention that Nogales et al. shows that FtsZ is an alpha/beta protein, it does not state that FtsZ comprises a Rossmann fold, or incorporate by reference the information in Nogales et al. The applicants note that claim 48 is an original claim, and at least one embodiment of claim 48 requires that the first molecule comprises a Rossmann fold (see claims 5-7, 16, and 17). Therefore the description at the time of filing does reasonably describe a FtsZ protein comprising a Rossmann fold, and this portion of the rejection for lack of written description has been deleted in this Office action relative to the rejection in the Office action mailed 16 February 2006.

The applicants assert that the disclosed genus of structures of first molecules and allosteric effectors describes the claimed species of methods of modulation of FtsZ without presenting any evidence that the disclosed genus includes the method of claims 35 and 48. The specification shows in Table 4 (pages 95-96), Table 5 (page 11), Table 6 (page 116), Table 7 (page 122), Table 8 (pages 95-96), and Table 9 (pages 140-141) that different first molecules are regulated by different allosteric effectors with different structures. Because no structure of an allosteric effector of FtsZ is described, the method of claims 35 and 48 are not described.

The applicants point to page 8, lines 20-21 and Example 20 (pages 142-143) as describing the methods of claims 35 and 48, however the cited passages do not show modulation of binding of FtsZ as required by the claims.

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The applicants assert that the facts in the instant application are distinguished from those in *University of Rochester v. G.D.Searle & Co.*, however in both the cited decision and the instant specification there is an absence of described structure of molecules recited in the claimed subject matter because the instant specification does not describe the structure of an FtsZ allosteric effector.

The applicants state that diarylamide allosteric effectors are described because amide means NR_2 . This Office action has an attachment of the definition of amide, which establishes that amide means NH_2 . Therefore, the applicant's arguments regarding description of claims 3-5, 7, 12-17, 20, 21, 26-29, 33-35, and 48 is not persuasive.

The applicants state that Hamilton et al. is not anticipatory because Hamilton et al. does not show the diaryl molecule binding to an allosteric site. However Hamilton et al. shows Mac-1, which is a allosteric molecule as defined in the specification, and Lee et al. shows that Mac-1 comprises a Rossmann fold and an I domain and comprises alpha helical and beta sheet domains. Hamilton et al. shows that Mac-1 binding is regulated by addition of diaryl compounds. The applicants have not provided evidence to show that Hamilton et al. is not anticipatory. The applicants point to Endemann et al. as showing that leumedins block an unknown process which is permissive for Mac-1 adherence (see abstract of Endemann et al.). However leumedins are not diaryl compounds or diarylamides (see Fig. 1 of Endemann et al.), and so the relationship of the action of leumedins to the claimed subject matter is not shown to exist by Endemann et al.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

John S. Brusca 6 November 2006
John S. Brusca
Primary Examiner
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jsb